WO 2005/070947 PCT/GB2005/000183

Claims

1. A method of synthesizing spongosine, which comprises reacting 1-O-acetyl-2,3,5-tri-O-benzoyl- β -D-ribofuranose with 2-methoxyadenine to form 9-(2',3',5'-tri-O-benzoyl- β -D-ribofuranosyl)-2-methoxyadenine, then deprotecting the 9-(2',3',5'-tri-O-benzoyl- β -D-ribofuranosyl)-2-methoxyadenine to form spongosine.

- 2. A method according to claim 1, wherein the 9-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-2-methoxyadenine is deprotected by treatment with sodium methoxide/methanol at room temperature.
- 3. A method according to claim 1 or 2, which further comprises suspending the spongosine in acetic acid, then isolating the spongosine.
- 4. A method according to claim 3, which further comprises dissolving the isolated spongosine in organic acid, then crystallizing the dissolved spongosine from the organic acid.
- 5. A method according to claim 1 or 2, which further comprises dissolving the spongosine in organic acid, then crystallizing the dissolved spongosine from the organic acid.
- 6. A method according to claim 4 or 5, wherein the organic acid is acetic acid.
- 7. A method according to any of claims 4 to 6, wherein the spongosine is crystallized from the organic acid by contacting the organic acid with an organic alcohol in which spongosine is partially soluble.
- 8. A method according to any preceding claim, which further comprises heating 2-chloroadenine with sodium methoxide/methanol at less than 150°C, preferably to 100°C, to form the 2-methoxyadenine.
- 9. A method of synthesizing 2-methoxyadenine, which comprises heating 2-chloroadenine with sodium methoxide/methanol to less than 150°C, preferably to 100°C.

WO 2005/070947 PCT/GB2005/000183

10. A method according to any of claims 1 to 7, which further comprises heating a mixture of 2-chloroadenine and sodium methoxide/methanol to form 2-methoxyadenine, adjusting the pH of the mixture to pH 9.5 (± 0.5), and isolating the 2-methoxyadenine before reacting the isolated 2-methoxyadenine with the 1-O-acetyl-2,3,5-tri-O-benzoyl- β -D-ribofuranose.

- 11. A method of synthesizing 2-methoxyadenine, which comprises heating a mixture of 2-chloroadenine and sodium methoxide/methanol to form 2-methoxyadenine, adjusting the pH of the mixture to pH 9.5 (±0.5), and isolating the 2-methoxyadenine.
- 12. A method according to claim 10 or 11, wherein the mixture is heated to less than 150°C, preferably to 100°C.
- 13. A method according to any of claims 8-12, which further comprises converting 2,6-dichloropurine to the 2-chloroadenine.
- 14. A method according to claim 13 in which the 2,6-dichloropurine is converted to 2-chloroadenine by treating the 2,6-dichloropurine with methanolic ammonia to produce 2-chloroadenine, diluting the 2-chloroadenine produced with water, and then isolating the 2-chloroadenine.
- 15. A method of synthesizing 2-chloroadenine, which comprises treating 2,6-dichloropurine with methanolic ammonia to produce 2-chloroadenine, diluting the 2-chloroadenine produced with water, and then isolating the 2-chloroadenine.
- 16. A method of synthesizing spongosine, which comprises the steps of Scheme 2.
- 17. A method of synthesizing spongosine, which is substantially as described with reference to Scheme 2.
- 18. A method of synthesizing 9-(2',3',5'-tri-O-benzoyl-β-D-rib ofuranosyl)-2-methoxyadenine, which comprises reacting 1-O-acetyl-2,3,5-tri-O-benzoyl-β-D-rib ofuranose

WO 2005/070947 PCT/GB2005/000183

with 2-methoxyadenine to form 9-(2',3',5'-tri-O-benzoyl- β -D-ribofuranosyl)-2-methoxyadenine.

- 19. Use of 2,6-dichloropurine in the synthesis of spongosine.
- 20. Spongosine that is at least 99% pure.